

Claims

1. An immortalized hepatocyte cell culture of human normal cell origin retaining an enzyme activity involved in the metabolism of xenobiotics in the liver or the capability of expressing a gene encoding an enzyme involved in the metabolism of xenobiotics in the liver.
- 5 2. The cell culture according to Claim 1 wherein the enzyme activity is NADPH cytochrome P450 reductase activity, glucuronosyl transferase activity, ethoxyresorufine dealkylation activity, benzyloxyresorufine dealkylation activity, pentoxyresorufine dealkylation activity, methoxyresorufine dealkylation activity, flavin monooxygenase activity, epoxy hydratase activity, 10 sulfotransferase activity or glutathione S-transferase activity.
- 15 3. The cell culture according to Claim 1 wherein the enzyme is NADPH cytochrome P450 reductase, NADPH cytochrome P450, flavin monooxygenase, epoxy hydratase, glucuronyl transferase, sulfotransferase or glutathione S-transferase.
- 20 4. The cell culture according to Claim 3 wherein the NADPH cytochrome P450 is CYP1A1, CYP1A2 or CYP3A.
5. The cell culture according to Claim 1 wherein the cell culture is FERM BP-6328.
- 25 6. A method of producing the cell culture according to Claim 1, characterized by introduction of the T antigen gene of SV (simian virus) 40 origin into human normal hepatocytes.
7. The production method according to Claim 6 wherein the 30 human normal hepatocytes are hepatocytes of human fetal origin.
8. A screening method for a compound or a salt thereof ① which inhibits or promotes an enzyme activity involved in the metabolism of xenobiotics in the liver or ② which 35 inhibits or promotes the expression of a gene encoding an enzyme involved in the metabolism of xenobiotics in the

liver, characterized by the use of the cell culture according to Claim 1.

9. A compound or a salt thereof ① which inhibits or promotes an enzyme activity involved in the metabolism of 5 xenobiotics in the liver or ② which inhibits or promotes the expression of a gene encoding an enzyme involved in the metabolism of xenobiotics in the liver, obtained by using the screening method according to Claim 8.

10. An analytical method for (a) enzymes involved in the 10 metabolism of xenobiotics and/or endogenous substrates, (b) metabolic pathways for xenobiotics and/or endogenous substrates, (c) chemical structures of metabolites of xenobiotics and/or endogenous substrates, (d) inhibition of enzymes which metabolize xenobiotics and/or endogenous 15 substrates, (e) promotion of the activity of enzymes which metabolize xenobiotics and/or endogenous substrates, (f) cytotoxicity due to the metabolism of xenobiotics and/or endogenous substrates, (g) genotoxicity due to the metabolism of xenobiotics and/or endogenous substrates, (h) 20 carcinogenicity due to the metabolism of xenobiotics and/or endogenous substrates, (i) mutagenicity due to the metabolism of xenobiotics and/or endogenous substrates, (j) hepatotoxicity due to the metabolism of xenobiotics and/or endogenous substrates, or (k) hepatic action of xenobiotics 25 and/or endogenous substrates, characterized by the use of the cell culture according to Claim 1.

11. A method of preparing metabolites of xenobiotics and/or endogenous substrates, characterized by the use of the cell culture according to Claim 1.